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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/537,710	03/30/2000	Anders Dahlqvist	3377/99-Util	9098

26474 7590 10/01/2003

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EXAMINER	
KERR, KATHLEEN M	

ART UNIT	PAPER NUMBER
1652	29

DATE MAILED: 10/01/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/537,710	DAHLQVIST ET AL.	
	Examiner	Art Unit	
	Kathleen M Kerr	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 July 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-23,25 and 28-35* is/are pending in the application.

4a) Of the above claim(s) *1-3,5-23,25,28,29 and 33-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Application Status

1. In response to the previous Office action, a written restriction requirement (Paper No. 21, mailed on February 9, 2003), Applicants filed an election and amendment received on July 15, 2003 (Paper No. 26). Said amendment cancelled Claim 4 and amended Claims 5, 6, 9-11, and 16, and added new Claims 33-34; a previous preliminary amendment had cancelled Claims 4, 26, and 27 (Paper No. 6 filed March 30, 2000). Thus, Claims 1-3, 5-23, 25, and 28-35 are pending in the instant Office action.

Election

2. Applicants' election with traverse of SuperGroup F (Claims 30-32), Group 1 (SEQ ID NOs: 1 and 2), in Paper No. 23 is acknowledged. The traversal is on the ground(s) that the restriction between the different sequences is improper; Applicants do not argue the restriction of the SuperGroups, just the Groups. Applicants argue that the Examiner's restriction does not conform to M.P.E.P. § 803.04 because up to ten sequences can be examined together and only in exceptional cases should restriction to a single sequence be made. This is not found persuasive because the claims are not drawn to nucleotide sequences having particular SEQ ID NOs; the claims are drawn to methods of using a nucleotide sequence that encodes a protein. When nucleotide sequences encoding proteins are claims, particularly according to the amino acid sequence, the search is much more extensive requiring additional resources in the Office. Thus, as noted in the M.P.E.P. § 803.04, "[a]bsent evidence to the contrary, each such nucleotide sequence is presumed to represent an independent and distinct invention, subject to a restriction

requirement pursuant to 35 U.S.C. § 121 and 37 C.F.R. § 1.141", and the "exceptional case" herein results from the encoding language that requires extensive searching.

The requirement is still deemed proper and is therefore made FINAL. Claims 1-3, 5-23, 25, and 28-35 are pending in the instant application. Claims 1-3, 5-23, 25, 28, 29, and 33-35 are withdrawn from further consideration as non-elected inventions. Claims 30-32, as they depend from non-elected Claims 7 and 16, will be examined herein with respect to the *S. cerevisiae* sequence (SEQ ID NOs: 1 and 2).

Priority

3. The instant application requests the benefit of priority for the foreign application 99106656.4 filed in Europe on April 1, 1999 in the declaration. No copy of this foreign document has been received, but it is not an official, ribboned copy. Without an official, ribboned copy, foreign priority cannot be granted.

The instant application is granted the benefit of priority for U.S. provisional applications 60/180,687 and 60/132,010 filed on February 7, 2000 and April 30, 1999, respectively, as requested in the declaration. The instant application is also granted the benefit for U.S. non-provisional application 09/329,802 filed on June 10, 1999 as requested in the declaration.

Information Disclosure Statement

4. No information disclosure statement has been filed with the instant application as of the date mailed of the instant Office action. Applicants are reminded that they have a duty to disclose all information, of which they are aware, relevant to the patentability of the pending claims (see 37 C.F.R. § 1.56 and M.P.E.P. § 2000).

Declaration

5. The oath filed on December 4, 2000 (Paper No. 5) is sufficient. However, no post office address is cited for Inventor Dahlqvist or Inventor Stymme as required by M.P.E.P. § 602 and 37 C.F.R. § 1.63. An application data sheet with this information will satisfy this requirement; Applicants are required to file such a sheet.

Drawings

6. The drawings are considered informal for the reasons detailed in the attached copy of PTO Form 948. Appropriate correction is required in response to the instant Office action and may not be held in abeyance (see 37 C.F.R. § 1.85(a)).

Compliance with the Sequence Rules

7. The sequence listing filed July 15, 2003 (Paper No. 26) has been entered. However, this application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to **fully** comply with the requirements of 37 C.F.R. § 1.821 through 1.825; Applicants' attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990).

a) On page 13, line 8, two oligonucleotides are disclosed without benefit of SEQ ID NO. If the noted sequences are in the sequence listing as filed, Applicants must amend the specification to identify the sequences appropriately by SEQ ID NO. If the noted sequences are not in the sequence listing as filed, Applicants must provide (1) a substitute copy of the sequence listing in both computer readable form (CRF) and paper copy, (2) an amendment directing its

entry into the specification, (3) a statement that the content of the paper and CRF copies are the same and, where applicable, include no new matter as required by 37 C.F.R. § 1.821 (e) or 1.821(f) or 1.821(g) or 1.821(b) or 1.825(d), and (4) any amendment to the specification to identify the sequences appropriately by SEQ ID NO.

8. In Applicants' amendment of the sequence listing (received July 15, 2003), no statement that the content of the paper and CRF copies are the same and, where applicable, include no new matter as required by 37 C.F.R. § 1.821 (e) or 1.821(f) or 1.821(g) or 1.821(b) or 1.825(d), was filed; such a statement is required.

Objections to the Specification

9. The specification is objected to for lacking complete continuity data in the first paragraph. The instant application claims the benefit of U.S. non-Provisional Application No. 09/329,802, filed on June 10, 1999 and now abandoned; however, no citation is noted in the first paragraph. Additionally, the benefit claim for 60/180,687 appears twice by virtue of amendments filed on May 1, 2000 and March 30, 2000. The May 1, 2000 amendment is proper; the March 30, 2000 amendment, citing the instant application as a continuation of the provisional application, is improper. Appropriate amendment to the specification is required wherein ---the instant application is a continuation (or continuation-in-part or divisional) of 09/329,802, filed on June 10, 1999 and now abandoned--- and ---the instant application claims benefit of U.S. Provisional applications 60/180,687 and 60/132,010 filed on February 7, 2000 and April 30, 1999, respectively--- (see M.P.E.P. § 201.11).

10. The specification is objected to for content placement. The description of the sequences and the description of the figures at the end of the specification (pages 30-37) should be moved to follow the Summary of Invention (insert above "General Methods" on page 12). Additionally, the section beginning "General Methods" on page 12 should be titles as ---Detailed Description of the Invention--- inserted above "General Methods". Correction is required.

11. In the Brief Description of the Drawings, the description of Figure 1 must be a description of Figures 1A and 1B. Similarly, of Figure 3 must be of Figures 3A, 3B, and 3C. Similarly, of Figure 4 must be of Figures 4A and 4B.

The Examiner also notes that Tables 1 and 2 are described in the Brief Description of the Figures and should be given Figure numbers as well as correcting "Tab" to ---Table---. Moreover, in Table 1, the commas should be periods to correctly display the data. Correction is required.

12. The specification is objected to because the title is not descriptive. A new title is required that is clearly indicative of the invention to which the elected claims are drawn (see M.P.E.P. § 606.01). The Examiner suggests the following new title:

---Methods of Making Triacylglycerol using Phospholipid:Diacylglycerol Acyltransferase---

13. In the specification, the Abstract is objected to for not completely describing the disclosed subject matter (see M.P.E.P. § 608.01(b)). It is noted that in many databases and in foreign countries, the Abstract is crucial in defining the disclosed subject matter, thus, its completeness is essential. The Examiner suggests the inclusion of the full name of the enzyme,

phospholipid:diacylglycerol acyltransferase, and the source species, *S, cerevisiae*, *S. pombe*, *A. thaliana*, *N. crassa*, *Z. mays*, and L. *esculentum*, for completeness. Correction is required.

14. The specification is objected to for being confusing for the following reasons:

a) In an amendment filed on July 15, 2003 (Paper No. 26), the amendment to page 4 describes SEQ ID NO:18 (in its first occurrence) as an amino acid sequence. SEQ ID NO:18 is a DNA sequence and must be described as such in the specification.
b) In an amendment filed on July 15, 2003 (Paper No. 26), the amendment to page 21, 3rd line, notes a correlation to SEQ ID NOs: 16-19 "respectively". The "respect" of this statement is unclear since the prior sentence notes SEQ ID NOs: 1-15.
c) In an amendment filed on July 15, 2003 (Paper No. 26), the amendment to page 21, last line, notes SEQ ID NO:12 is an amino acid. This is incorrect since SEQ ID NO:12 is an *L. esculentum*, DNA sequence.

Correction and/or clarification for each of these are required.

15. The amendment filed July 15, 2003 (Paper No. 26) is objected to under 35 U.S.C. § 132 because it introduces new matter into the disclosure. 35 U.S.C. § 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: "the master gene" in Claim 29. This appears to be a typographical error and should be ---marker gene--- which has clear support in the specification as originally filed. Applicant is required to cancel or amend the new matter in the reply to this Office Action.

Objections to the Claims

16. Claims 30-32 are objected to for containing non-elected subject matter. Claim 7 is not limited to the elected sequences, SEQ ID NOs: 1 and 2, from *S. cerevisiae*. Amendment is required.

17. Claims 30-32 are objected to for depending from non-elected claims. All the limitations of Claims 7 and 16 must be amended into Claims 30-32 so that they stand alone.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

18. Claim 30 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "transgenic cell or organism" is unclear. Must the organism also be transgenic? By virtue of the specification, it seems that both the cell and the organism must be transgenic; however, this limitation cannot be read into the claims. Correction and/or clarification are required.

19. Claim 30 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In lines 6-8, the "whereby" phrase is wholly unclear without a verb and redundant since this limitation is found both prior to this phrase in the claim and in the parent claim, Claim 16 as it depends from Claim 7. Correction and/or clarification are required.

20. Claims 31-32 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "using **the** nucleotide sequence of claim 7" (emphasis added) is unclear since the "the" refers to a particular sequence and Claim 7 encompasses to an

entire genus of nucleotide sequences. The article should be ---a--- or should be drawn to a specific nucleotide sequence. Correction and/or clarification are required.

21. Claims 31-32 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "uncommon" is unclear as to its metes and bounds. The specification is unclear as to whether this term defines a particular set of fatty acids or if this term is a relative term. If the term is describing a particular set of fatty acids, which are included? If the term "uncommon" is a relative, the claims are rendered indefinite because the term "uncommon" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

22. Claim 31 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "preferably, increased" renders the claim indefinite because it is unclear whether the limitations following the word are part of the claimed invention. See M.P.E.P. § 2173.05(d). Moreover, the comma should be after increased and not around preferably. Correction and/or clarification are required.

23. Claim 32 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The instant claim is confusing because it is drawn to a method having no specific method steps. Correction and/or clarification are required.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

24. Claims 30-32 are rejected under 35 U.S.C. § 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 30-32 are drawn to methods using transgenic cells having a nucleotide sequence that encodes an enzyme that is claimed solely by function and without any structural limitations.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." University of California v. Eli Lilly and Co., 1997 U.S. App. LEXIS 18221, at *23, quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these.

In the instant specification, a novel enzyme activity is described as phospholipid: diacylglycerol transferase (PDAT). Some plants, and not others, have this activity (see page 16 of the instant specification). A yeast gene, YNR008w, was tested for this activity and was confirmed to be a PDAT that can be overexpressed in yeast and *A. thaliana* to increase fatty acid content in cells. The specification also describes numerous shorter DNA's and encoded proteins putatively described as PDAT genes; however, no testing on these gene fragments has been performed to confirm the proposed function. Thus, one species of the claimed genus has been fully described, that is the use of the *S. cerevisiae* sequence (SEQ ID NOs: 1 and 2) to produce transgenic organisms with increased triacylglycerol production. No relationship between this species and the structures of the other proposed species is described. No relationship between the structure and function of the disclosed species, *S. cerevisiae*, is described. No common characteristics, other than the enzyme function, is required in the claims. Thus, one of skill in the art would be unable to predict the structure of other members of this genus based on of the instant disclosure.

The Examiner suggests limiting the instant methods to use of a polynucleotide with a structure specifically related to SEQ ID NO:1 (or a DNA encoding SEQ ID NO:2), such as 95% identical to SEQ ID NO:1, wherein the DNA encodes a PDAT.

25. Claims 30-32 are rejected under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for methods of making triacylglycerol using a host organism transformed with a gene encoding PDAT from *S. cerevisiae* (SEQ ID NO:1), does not reasonably provide enablement for methods using any gene encoding any PDAT from any source absent any structural limitations. The specification does not enable any person skilled in

the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. To find additional PDAT genes and use them in the claimed methods would require undue experimentation.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

In the instant specification, a novel enzyme activity is described as phospholipid: diacylglycerol transferase (PDAT). Some plants, and not others, have this activity (see page 16 of the instant specification). A yeast gene, YNR008w, was tested for this activity and was confirmed to be a PDAT that can be overexpressed in yeast and *A. thaliana* to increase fatty acid

content in cells. The specification also describes numerous shorter DNA's and encoded proteins putatively described as PDAT genes; however, no testing on these gene fragments has been performed to confirm this function.

The instant specification proposes 5 additional species of PDAT genes (6 total) and provides guidance and working examples to test for their activity. However, the nature of the invention is that genes encoding PDAT must be known to practice the claimed invention; the prior art provides none of these with respect to structure and related function. Due to the lack of a structure/function correlation analysis of the yeast PDAT gene, proven to function as a PDAT in the instant specification, it is wholly unpredictable which of the disclosed fragments of yeast and plant sequences encode additional PDATs. Moreover, the full-length sequences are not disclosed; only ESTs are disclosed. While a skilled artisan could find additional full length sequences using the disclosed ESTs and functional assays, the ability to find does not fulfill the statutory requirement of the ability to make. Having the instant disclosure in full view of the prior art, one of skill in the art would be unable to predict the structure of PDAT genes so as to be able to make them, even in the likeness of SEQ ID NO:1 (the *S. cerevisiae* sequence). Thus, the instant claims are not enabled to the full extent of their scope.

26. Claims 31-32 are rejected under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for methods to produce triacylglycerol, does not reasonably provide enablement for methods to produce triacylglycerol with uncommon fatty acids in organisms without the ability to natively produce triacylglycerol with uncommon fatty acids. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

To make some cells that produce TAG with uncommon fatty acids would require undue experimentation.

The factors to be considered in determining whether undue experimentation is required are summarized above.

On page 1 of the specification, the invention as described as being able to produce uncommon fatty acids "in combination with a gene for the synthesis of an uncommon fatty acid"; the PDAT gene does not regulate this process. Thus, to effectively practice the claimed methods, one would be required to use organisms that naturally produce uncommon fatty acids or to use organisms also transformed with a gene for the synthesis of an uncommon fatty acid. The specification provides no guidance or working examples for producing uncommon fatty acids in the absence of uncommon fatty acid genes (either endogenous or exogenous). Thus, the instant claims are not enabled to the full extent of their scope.

27. Claim 31 is rejected under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for methods to produce triacylglycerol and other fatty acids, does not reasonably provide enablement for methods to produce host cells with increased overall oil content. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. To make some cells with increased oil production would require undue experimentation.

The factors to be considered in determining whether undue experimentation is required are summarized above.

The instant specification describes methods that increase the fatty acid content of host cells wherein a PDAT gene is overexpressed (see page 19 and Table 2); the instant specification does not describe increasing the overall oil content of the host organism, which is a distinct method. As noted in WO96/38573 on page 1, "[c]urrently, there are no documented demonstrations of increased in oil content by transgenic means...[i]n contrast, increased in the proportions of some strategic fatty acids have been achieved by the introduction of various plant fatty acid biosynthesis and acyltransferase genes in oilseeds." The state of the art provides no examples to support the scope of the claimed invention. Thus, in the claim is not enabled to the full extent of its scope.

Claim Rejections - 35 U.S.C. § 101

35 U.S.C. § 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

28. Claims 30 and 32 are rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter. Claims 30 and 32, as written, do not sufficiently distinguish over cells as they naturally exist because the claims do not particularly point out any non-naturally occurring differences between the claimed products used in the methods and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See Diamond v. Chakrabarty, 447 U.S. 303, 206, USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g. by insertion of "isolated" or "purified". See M.P.E.P. § 2105.

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

29. Claims 30 and 32 are rejected under 35 U.S.C. § 102(b) as being anticipated by **Yu** *et al.* (Molecular Cloning and Characterization of Two Isoforms of Saccharomyces cerevisiae Acyl-CoA:Sterol Acyltransferase. J. Biol. Chem. (1996) 271(39):24157-24163) as evidenced by **Dahlqvist** *et al.* (Phospholipid:diacylglycerol acyltransferase: An enzyme that catalyzes the acyl-CoA-independent formation of triacylglycerol in yeast and plants. PNAS (2000) 97(12):6487-6492). The instant claims are drawn to methods of making triacylglycerol (TAG) using a transgenic organism that contains and expresses a phospholipid:diacylglycerol transferase (PDAT) gene.

Yu *et al.* teach expression of human ACAT (acyl-CoA:cholesterol acyltransferase) in yeast cells (see page 24162). As taught by Dahlqvist *et al.*, yeast cells inherently contain and express a PDAT gene and inherently produce TAG; thus, the expression of any gene in transgenic yeast meets all the limitations of Claim 30. Moreover, since the yeast cells used by Yu *et al.* inherently contain a PDAT gene, all the limitations of Claim 32 are met.

Claim Rejections - 35 U.S.C. § 103

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

30. Claim 31 is rejected under 35 U.S.C. § 103(a) as being unpatentable over the combination of **Verhasselt** *et al.* (Twelve open reading frames revealed in the 23.6 kb segment flanking the centromere on the *Saccharomyces cerevisiae* chromosome XIV right arm. Yeast (1994) 10(10):1355-1361) and **Zou** *et al.* (WO 96/38573). The instant claims is drawn to methods of making triacylglycerol (TAG) by transforming a cell with a phospholipid: diacylglycerol transferase (PDAT) gene wherein the fatty acid content of the cell is altered.

Verhasselt *et al.* teach ORF N2042 from *S. cerevisiae* (see attached GenBank reference CAA54576 related to paper) that is identical to the *S. cerevisiae* PDAT gene (SEQ ID NO:1) from the instant application. Verhasselt *et al.* further teach that N2042 encodes a putative phosphatidylcholine-sterol O-acyltransferase (see page 1358). Verhasselt *et al.* do not teach expression of N2042 in a host organism or alteration of the fatty acid content of said host organism.

Zou *et al.* teach methods of altering the oil content of plants by transforming said plant with a yeast gene encoding an acylglyceride fatty acyltransferase (see page 3). Moreover, Zou *et al.* teach numerous examples of how overexpression of various acyltransferases related to sterol biosynthesis increases fatty acid production in cells (see page 2).

It would have been obvious to one of ordinary skill in the art at the time of the invention to express the O-acyltransferase taught by Verhasselt *et al.* in a host cell for the increased production of fatty acids because Verhasselt *et al.* describe the ORF as an O-acyltransferase and there are numerous acyltransferases being overexpressed in host cells to increase fatty acid production as taught by Zou *et al.* One would have been motivated to combine the prior art to produce a higher fatty acid yielding organism due to the commercial market of see oils (see page 1 of Zou *et al.*). One would have had a reasonable expectation of success that introduction of the sterol O-acyltransferase of Verhasselt *et al.* into the methods of Zou *et al.* would have produced a host organism with an altered fatty acid content due to the numerous examples taught by Zou *et al.*

Additionally Cited References

31. The following are cited to complete the record; they are not considered prior art against the claims:

a) Sorger *et al.* Triacylglycerol biosynthesis in yeast. Appl. Microbiol. Biotechnol. (2003) 61:289-299.

b) Oelkers *et al.* A Lecithin Cholesterol Acyltransferase-like Gene Mediates Diacylglycerol Esterification in Yeast. J. Biol. Chem. (2000) 275(21):15609-15612.

Conclusion

32. Claims 30-32 are not allowed for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (703) 305-1229. The examiner can normally be reached on Monday through Friday, from 8:30am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy can be reached on (703) 308-3804. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

KMK
September 29, 2003